Varicella Zoster and the Older Adult

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2013 Pennsylvania Coalition of Nurse Practitioners
11/9/13

Objectives
- Discuss the incidence of varicella zoster virus, commonly affected dermatomes and reactivation risk factors
- State common signs and symptoms of varicella zoster virus and discuss possible differential diagnosis
- State at least two of anti-viral medications and dosages used to treat varicella zoster virus
- List clinical indications and contraindications for live attenuated varicella zoster virus
- Discuss management of pain in varicella zoster virus in the acute and post acute phase

Scope of the Problem
- On average 1.1 million people in the United States will develop herpes zoster annually
- The number of cases will rise as the population ages and more people are living with immunocompromizing conditions such as hepatitis, AIDS, solid organ transplants and post cancer treatment.
- It is an extremely painful condition and is known to have a many as 175 documented complications
- Research has shown that 1 in 4 persons affected will develop one or more complications
- Any complication more than doubles the cost of care
- The cost of treating Herpes zoster infections in the US is estimated at $1.1 billion annually

VZV [varicella zoster virus]

Incidence of VZV
- Age at time of primary infection is important. If infection occurs intrauterine or very early childhood, there is 35% higher risk of another VZV infection by age 12
- By adulthood, 98% of the population of the US will have acquired the VZV virus
- 1 in 3 persons will develop herpes zoster
- Women have slightly higher statistical risk of acquiring herpes zoster
- Blacks have significantly lower risk of developing herpes zoster

Human alpha-herpes virus - causes varicella (chickenpox) and herpes zoster (shingles)
Initial infection with VZV leads to chicken pox
After recovery from chicken pox the VZV becomes dormant in the dorsal root ganglia
VZV can reactivate at any time.
In 1995 the first vaccination for varicella was licensed
In 2006 a combination vaccine containing live attenuated measles, mumps, rubella and varicella virus was licensed Recommended for ≥ 12 months

VZV
- After primary exposure, infected cells carry the virus to T cells within lymph nodes to the sensory ganglia
- Dormant varicella virus has been detected in cranial, cervical, thoracic, lumbosacral ganglia.
- When reactivation occurs, virions are formed on the involved sensory nerves
- These virions spread through axons and along the dermatomes of the sensory nerves to the epidermis.
- The result is a vesicular rash along a single or several closely grouped dermatomes.
- The most commonly involved sites are the thoracic nerves and the ophthalmic branch of the trigeminal nerve
Risk Factors for Reactivation of VZV

Aging is the single highest risk factor for the development of Herpes zoster
- Cell mediated immunity declines
- Immune senescence
- Significant increase in risk for reactivation starts between age 50 -60
- 50% of all adults will have had an episode of herpes zoster by age 85

Additional Risk Factors for Reactivation

- Endogenous Boosting
- Household Exposure
- Immunosuppression
  - Hematologic malignancy
  - Solid tumors
- Chronic Diseases
- Solid Organ Transplant
- Stem Cell Transplant
- Immunization with VZV vaccine [MMR]
- Stress

Clinical Presentation

- Symptoms occur several days to weeks before the rash is visible
- Prodromal symptoms are common
  - Pain, burning, and itch along a unilateral dermatome are most common
  - Over 80% of patients have reported pain preceding the rash of herpes zoster
  - Headache, fatigue, photophobia and less commonly fever can also precede the rash
- Typically the rash begins as erythematous macules that develop into vesicles, then into clusters or crops of vesicles. These vesicles evolve to pustules, ulcers and finally crusts
- The virus creates vesicles long a unilateral dermatome of the dorsal root or the cranial nerve ganglia
- The incubation period is 10 to 21 days, with the most infectious period of time being five days before the appearance of the rash
- The infectious period continues until all the vesicles have dried and crusted over.
- The immunocompetent individual will have crusting of the lesions within 7 to 10 days
- Rarely herpes zoster occurs without a rash - Zoster Sine Herpete
Diagnosis

- Diagnosis is most commonly made based on clinical presentation
- Differential may include:
  - papular urticaria, contact dermatitis, scabies or other insect bites, impetigo, drug eruption, or folliculitis.
- Diagnostic challenges
  - atypical presentations
  - previously unexposed individuals acquire VZV.
  - Repeat outbreaks of shingles.

- For difficult diagnosis
  - Tzanck smear of vesicular fluid can conclusively show multinucleated giant cells thereby confirming the diagnosis

  - CDC National VZV Laboratory Services - The National VZV Laboratory can provide several types of VZV-specific testing free-of-charge to state and local public health departments who require confirmatory evidence for VZV infection or confirmation of atypical herpes zoster cases, and to physicians and scientists participating in various epidemiologic and laboratory-based studies.

  www.cdc.gov/shingles/downloads/vzv_lab_services.pdf

How to do a Tzanck Smear

- Unroof intact vesicle and scrape the base
- Smear gently on clean slide and allow to air dry
- Apply Toluidine blue, let sit for 60-90 seconds
- Rinse gently under water and blot dry
- Apply immersion oil to view under microscope
- Look for multinucleated giant cells

Managing the Acute Infection

- Early recognition and treatment are critical to limiting the extent of the infection
- Oral antivirals are the cornerstone of treatment: Acyclovir, Famciclovir or Valacyclovir
  - Acyclovir – 800mg five times a day for 7-10 days
    - Estimated cost for generic – $29-$41
  - Famciclovir – 500mg three times a day for 7 days
    - Estimated cost for generic – $228
  - Valacyclovir – 1 gm three times a day for 7 day
    - Estimated cost for generic – $221
  - Some evidence suggests famciclovir and valacyclovir are superior in reducing prolonged pain
  - In recalcitrant cases intravenous acyclovir is necessary – 10mg/kg every 8 hours for 7 days

- Managing Acute Pain

  - Managing pain is critical to care of patients with herpes zoster
  - First line treatment for mild to moderated pain is acetaminophen or non-steroidal anti-inflammatory medications
  - Tramadol or codeine can be used for moderated pain
  - Opioid analgesics may be needed for severe pain in the first 2-3 weeks of the outbreak
  - Gabapentin and tricyclic antidepressants have not been found to reduce acute pain in herpes zoster
Managing Acute Pain

- Adding corticosteroids to antivirals may reduce acute pain and time to healing.
- Avoid adding corticosteroids to regimen if patients have risk for steroid related toxicity: Diabetes mellitus, gastritis, Hepatitis B, solid organ transplant recipients.
- Usual dose for steroids if indicated is 3 week tapering dose.
- Epidural nerve blocks.
- Percutaneous electrical nerve stimulation - 3 time week for 2-3 weeks.
- Topical capsaicin or lidocaine.
- Acupuncture.

Acute Complications

- Impetigo - bacterial skin infection secondary to scratching.
  - Keep site cool and dry to help reduce the pruritis that leads to intense scratching.
  - Cover rash sites when out with others, otherwise leave uncovered to allow vesicles to dry.
  - Treat with mupirocin 2% topically if limited area is affected.
  - Add oral antibiotic for more extensive areas. Cephalexin, dicloxacillin or clindamycin are effective against S. aureus and methicillin-resistant S. aureus.

Acute Complications

- Herpes zoster ophthalmicus
  - Accounts for 10-20% of all VZV outbreaks.
  - Prodromal phase includes:
    - Headache
    - Fever
    - Malaise
    - Pain in the affected eye.
  - Acute symptoms include:
    - Hutchinson sign - early lesion/vesicle on tip or nose or side of nose.
    - Vesicular rash along the ophthalmic branch of trigeminal nerve.
    - Hyperemic conjunctivitis.
    - Epiphora and lid droop.
    - Facial scarring and cranial nerve palsies may also occur.
  - Start antivirals early and place urgent consult to ophthalmology - facial scarring, cranial nerve palsies and loss of vision can occur.

Acute Complications

- Ramsay Hunt Syndrome - also termed herpes zoster oticus.
  - Affects the ear canal, auricle, mucous membrane of the oropharynx, hard palate and tongue. Symptoms may include; headache, vertigo, deafness, tinnitus, facial paralysis and loss of taste.
  - Of patients presenting with lower motor neuron facial palsy, 12% have RHS; the diagnosis can be missed if there is no rash.
Acute Complications

• Neurologic Complications
  – Encephalitis
  – Myelitis
  – Aseptic meningitis
  – Guillain Barré syndrome
  – Hemiparesis
  – Cranial/peripheral nerve palsies
• Acute retinal necrosis
• Disseminated herpes zoster
  – Systemic dissemination lead to visceral involvement of lung, liver and brain
  – If visceral dissemination occurs mortality rates are as high as 15%

Rare Complication – Pseudo-hernia

• There have been rare cases of abdominal distension and pseudo-hernia causes by Herpes Zoster
• Resolution occurred in 2-3 months with pain management. Work-up for internal organ involvement is indicated

Post Herpetic Rash Complications

• Complications are very common. As many as 175 complications have been documented as result of Herpes zoster
• One population based study found that one in four persons with shingles experienced a complication
• The most common complication is pain lasting longer than the rash
• Post Herpetic Neuralgia (PHN) is defined as pain lasting beyond the period of infection. Usually greater than 30 days
• PHN occurs in 10-18% of persons with Shingles
• The pain can be constant, intermittent, or triggered by a common stimulus such as touch, cold or warmth.

Post Herpetic Neuralgia

• Higher risk for PHN include:
  – Women
  – Elderly
  – Individuals presenting severe rash and pain
  – Those with prodromal pain
  – Those with ophthalmic involvement.
• Tricyclic antidepressants (TCA’s) are the mainstay of PHN therapy.
  – Inhibit the nociceptive signals from the periphery.
  – May take up to three weeks to reduce the pain
• Anticholinergic side effects are often poorly tolerated and contraindicated in the elderly

Post Herpetic Neuralgia

• Most commonly used TCA is nortriptyline
  – start with 25mg at HS. Increase every 2-3 days as tolerated to maximum of 150mg (if needed)
• Gabapentin
  – Start with 300mg at HS and increase every 2-3 days as tolerated to maximum of 3600mg if needed
• Pregabalin
  – Start with 75mg at bedtime and increase to 600mg if needed

Studies show that anticonvulsants reduce PHN pain by 50%

Special Populations

• Persons with Ostomies
• Persons with IBD
• Persons with Vitiligo
• Persons with Psoriasis
Special Populations

• Ostomates
  – 30-40% of herpes zoster outbreaks are truncal
  – For vesicles on or very near a stoma:
    • Topical acyclovir may help dry and resolve lesions faster
    • Try not to cover the lesions. If possible cut out wedge to avoid covering the vesicles. Seal cut out edge with waterproof tape
    • Ostomy powder can help to dry the lesions
    • Try to cover the affected area with a silicone absorbent dressing, or polyurethane foam dressing

• Inflammatory Bowel Disease
  – There is a significantly higher number of reports of disseminated VZV in persons with IBD
  – This may be because of the common use of combination immunosuppressive medications in treatment of IBD
  – This population should be screened for VZV exposure/immunity and vaccinated prior to immunosuppression

• Vitiligo
  – Case reports have shown that VZV rash can cause de-pigmentation at site of rash but in those with vitiligo it can trigger further de-pigmentation in other areas as well

• Psoriasis
  – areas of VZV rash can cause stimulate Koebner phenomenon. Isomorphic reaction that leads to new psoriatic lesions at site of trauma

Prevention

• ACIP recommends zoster vaccine live for all adults aged 60 or older [Advisory Committee on Immunization Practices]
  • In 2006 zoster vaccine live [Zostavax®] was licensed to prevent shingles in immunocompetent adults
  • Though transmission of the virus is possible between the vaccinated person and susceptible contacts - Shingles Prevention Study of 7,500 persons observed for 4 years showed no transmission of virus from the vaccine
  • Offer at first clinical encounter
  • Administer 0.65ml subcutaneously in deltoid region of the arm
  • Vaccination is not indicated for:
    – those with allergy to gelatin or neomycin
    – Pregnant or breast feeding women
    – Severe immunosuppression

• VarIZIG is a varicella zoster immune globulin
  • Approved in 2011 by FDA for persons
    – With no evidence of immunity to VZV (never had chickenpox or vaccination)
    – Who are at high risk for severe disease and it’s complications, and have been exposed to VZV
  • Typically given to exposed premature infants, neonates, pregnant women, and the severely immune-compromised person
  • Initially approved for up to four days after exposure, this period has been extended to ten days by the FDA.

  • It is administered intramuscularly and can be obtained through the sole U.S. distributor, FFF Enterprises. 24 hours a day at 1-800-843-7477 or via the internet at http://www.fffenterprises.com

• Shingles Support Groups
  – http://www.mdjunction.com/shingles
  – http://www.coolmommy.org/6/shingles/support-group
  – http://www.shinglesight.org/content/pub/shingles-support-society

• Acute Pain Foundation (APF)
  – P.O. Box 850
  – Rocklin, CA 95677-0850
  – Tel: 916-632-0222; 800-533-3231
  – Fax: 916-652-8190

• National Shingles Foundation [For Research on Varicella Zoster]
  – 603 W. 115 Street
  – Suite 321
  – New York, NY 10025
  – Tel: 212-222-3390
  – Fax: 212-838-0380

Resources